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10/535,084	06/08/2006	Claus Harder	117163.00137	8537

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EXAMINER	
FRAZIER, BARBARA S	
ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/535,084	HARDER ET AL.	
	Examiner	Art Unit	
	BARBARA FRAZIER	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 7-23* is/are pending in the application.

4a) Of the above claim(s) *1-3,8,10,11 and 16-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,7,9 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-4 and 7-23 are pending in this application.

2. Claims 5, 6, 24, and 25 stand canceled.

3. Claims 1-3 and 19-23 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/22/08.

4. Claims 8, 10, 11, and 16-18 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/22/08.

5. Claims 4, 7, 9, and 12-15 are examined.

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Double Patenting

7. **Claims 4, 7, 9, 12-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 and 21-24 of copending Application No. 10/706,717.** Although the

conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same subject matter and composition components.

The claimed invention is drawn to a pharmaceutical formulation comprising yttrium (Y), neodymium (Nd), or zirconium, adapted to be implanted in a vascular vessel and adapted to inhibit the proliferation of human smooth muscle cells of the vascular vessel wherein the formulation is adapted for intravascular liberation after implantation in a vascular vessel and the formulation includes an at least very substantially biodegradable carrier (see claim 4).

The '717 application is drawn to an endoprosthesis comprising a carrier structure comprising a metallic material, which comprises a magnesium alloy of the following composition:

Magnesium:	>90%
Yttrium:	3.7% - 5.5%
Rare earths:	1.5% - 4.4% and
Balance:	<1%.

The "rare earths" may comprise neodymium (claim 4) and the "balance" may comprise zirconium (claim 5).

The '717 application differs from the claimed invention because it is named as an endoprosthesis, and because it does not recite the limitations of "pharmaceutical formulation" and "inhibiting the proliferation of human smooth muscle cells wherein the formulation is adapted for intravascular liberation after implantation in a vascular vessel".

However, the limitations in the claimed invention of are intended use and do not lend patentable weight to the composition as claimed. Furthermore, the intended use of the '717 application as "endoprosthesis" does not lend patentable weight to the composition as claimed. Therefore, the composition of the claimed invention and the '717 application are drawn to the same subject matter and composition components.

With respect to the dependent limitations of amounts of metals present, the '717 application teaches ranges which are encompassed by, or comparable to, the ranges taught in the claimed invention, and one skilled in the art would select optimal amounts of metals as a matter of routine experimentation.

With respect to the yttrium concentration in the region of the human smooth muscle cells to be treated (claim 15), the '717 application would be capable of adapting to provide such a concentration, especially given the fact that the amount of yttrium taught in the '717 application is encompassed by the amount of yttrium taught in the claimed invention. The limitation is one of intended use, and does not lend patentable weight to the composition as claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. **Claims 4, 7, 9, and 12-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5, 7-9, and 16-19 of copending Application No. 10/596,797.** Although

the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same subject matter and composition components.

The claimed invention is recited above (see paragraph 7).

The '797 application is drawn to a radiopaque marker for medical implants comprising 10 to 90 wt.% of a biodegradable base component, 10 to 90 wt.% of one or more radiopaque elements including Y and Nd, less than or equal to 10 wt.% residual components, the components cited adding up to 100 weight-percent. The biodegradable base component may be a magnesium alloy (claim 3). The definition of "residual components" in the '797 application includes Zr, and the definition of "magnesium alloy" includes WE43 (see paragraph 27, page 8).

The '797 application differs from the claimed invention because it recites the limitation of "radiopaque marker for medical implants", and it does not recite the limitations of "pharmaceutical formulation" and "inhibiting the proliferation of human smooth muscle cells wherein the formulation is adapted for intravascular liberation after implantation in a vascular vessel".

However, the limitations in the claimed invention are intended use and do not lend patentable weight to the composition as claimed. Furthermore, the intended use of the '797 application as "radiopaque marker for medical implants" does not lend patentable weight to the composition as claimed. Therefore, the composition of the claimed invention and the '797 application are drawn to the same subject matter and composition components.

With respect to the dependent limitations of amounts of metals present, the '797 application teaches ranges which are comparable to the ranges taught in the claimed invention, and one skilled in the art would select optimal amounts of metals as a matter of routine experimentation.

With respect to the yttrium concentration in the region of the human smooth muscle cells to be treated (claim 15), the radiopaque marker of the '797 application would be capable of adapting to provide such a concentration, especially given the fact that the amount of yttrium taught in the '797 application is comparable to the amount of yttrium taught in the claimed invention. The limitation is one of intended use, and does not lend patentable weight to the composition as claimed.

9. **Claims 4, 7, 9, and 12-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 and 11 of copending Application No. 10/908,729.** Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same subject matter and composition components.

The claimed invention is recited above (see paragraph 7).

The '729 application is drawn to an implant for vessel ligature comprising an alloy which is at least partially biodegradable and which comprises:

greater than 87% magnesium;

from about 3% to about 6% yttrium;

from about 1% to about 5% lanthanide; and

a balance of about 0.0% to about 2%.

The "lanthanide" further comprises neodymium (claims 4 and 5), and the "balance" further comprises zirconium (claims 7-9 and 11).

The '729 application differs from the claimed invention because it recites the limitation of "implant for vessel ligature", and it does not recite the limitations of "pharmaceutical formulation" and "inhibiting the proliferation of human smooth muscle cells wherein the formulation is adapted for intravascular liberation after implantation in a vascular vessel".

However, the limitations in the claimed invention are intended use and do not lend patentable weight to the composition as claimed. Furthermore, the intended use of the '797 application as "implant for vessel ligature" does not lend patentable weight to the composition as claimed. Therefore, the composition of the claimed invention and the '729 application are drawn to the same subject matter and composition components.

With respect to the dependent limitations of amounts of metals present, the '729 application teaches ranges which are encompassed by or comparable to the ranges taught in the claimed invention, and one skilled in the art would select optimal amounts of metals as a matter of routine experimentation.

With respect to the yttrium concentration in the region of the human smooth muscle cells to be treated (claim 15), the implant of the '729 application would be

capable of adapting to provide such a concentration, especially given the fact that the amount of yttrium taught in the '797 application is encompassed by or comparable to the amount of yttrium taught in the claimed invention. The limitation is one of intended use, and does not lend patentable weight to the composition as claimed.

10. **Claims 4, 7, 9, and 12-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application No. 11/221,322 and claims 1-4 of copending Application No. 11/221,344.** Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same subject matter and composition components.

The claimed invention is recited above (see paragraph 7).

The '322 application and the '344 application are drawn to an endoprosthesis comprising a magnesium alloy of the following composition:

Magnesium:	between about 60.0 and about 88.0% by weight
Rare earth metals:	between about 2.0 and about 30.0% by weight
Yttrium:	between about 2.0% and about 20.0% by weight
Zirconium:	between about 0.3% and about 5.0% by weight
Balance:	between 0 and about 10.0% by weight

The '322 application also comprises neodymium in claims 3 and 4; the '344 application also comprises neodymium in claim 1.

The '322 application and the '344 application differ from the claimed invention because they recite the limitation of "endoprosthesis comprising a carrier structure", and they do not recite the limitations of "pharmaceutical formulation" and "inhibiting the proliferation of human smooth muscle cells wherein the formulation is adapted for intravascular liberation after implantation in a vascular vessel".

However, the limitations in the claimed invention are intended use and do not lend patentable weight to the composition as claimed. Additionally, the presence of a "carrier structure" in the '322 and '344 applications is not excluded from the pharmaceutical formulation of the claimed invention. Furthermore, the intended use of the '322 and '344 applications as "endoprosthesis" does not lend patentable weight to the composition as claimed. Therefore, the composition of the claimed invention and the '322 and '344 applications are drawn to the same subject matter and composition components.

With respect to the dependent limitations of amounts of metals present, the '322 and '344 applications teach ranges which are encompassed by or comparable to the ranges taught in the claimed invention, and one skilled in the art would select optimal amounts of metals as a matter of routine experimentation.

With respect to the yttrium concentration in the region of the human smooth muscle cells to be treated (claim 15), the endoprosthesis of the '322 application and the '344 application would be capable of adapting to provide such a concentration, especially given the fact that the amount of yttrium taught in the '322 and '344 applications is encompassed by or comparable to the amount of yttrium taught in the

claimed invention. The limitation is one of intended use, and does not lend patentable weight to the composition as claimed.

Response to Arguments

11. Applicants have requested that consideration of the provisional rejections of claims 4, 7, 9, and 12-15 on the ground of nonstatutory obviousness-type double patenting be deferred until the patentability of any of the cited co-pending applications has been determined. Applicant's request is acknowledged; however, since all of the copending applications are still being considered for patentability, the provisional rejections stand.

Claim Rejections - 35 USC § 102

12. Claims 4, 7, 9, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Stroganov et al., US Patent 3,687,135.

The claimed invention is drawn to a pharmaceutical formulation comprising one or more of the elements from the group yttrium (Y), neodymium (Nd), or zirconium (Zr), adapted to be implanted in a vascular vessel and adapted to inhibit the proliferation of human smooth muscle cells of the vascular vessel wherein the formulation is adapted for intravascular liberation after implantation in a vascular vessel and the formulation includes an at least very substantially biodegradable carrier (see claim 4).

In the elected species of the claimed invention, the element is yttrium and the biodegradable carrier is a magnesium alloy.

Stroganov et al. teach a magnesium-base alloy for use in bone surgery which contains the following components, wt. % (see abstract):

Rare earth metal	0.40–4.0
Cadmium	0.05–1.2
Calcium or aluminum	0.05–1.0
Manganese	0.05–1.0
Silver	0–0.8
Zirconium	0–0.8
Silicon	0–0.3
Magnesium	remainder

Stroganov et al. further teach that neodymium and yttrium are predominantly employed as the rare earth metal (col. 2, lines 29-31). A magnesium alloy comprising yttrium at 1.6 wt.% is exemplified (see Example 3). The limitations in the claim of "adapted to be implanted in a vascular vessel and adapted to inhibit the proliferation of human smooth muscle cells of the vascular vessel" are not given patentable weight, since the composition of Stroganov et al. has pharmaceutical use in bone surgery, and thus would be capable of the intended use of the claimed invention. Therefore, the composition of Stroganov et al. anticipates the composition of the claimed invention.

With respect to the yttrium concentration in the region of the human smooth muscle cells to be treated (claim 15), the composition of Stroganov et al. would be capable of adapting to provide such a concentration, especially given the fact that the amount of yttrium taught by Stroganov et al. is encompassed by the amount of yttrium taught in the claimed invention. The limitation is one of intended use, and does not lend patentable weight to the composition as claimed.

Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a

claim or claim limitation; "adapted for" clauses are an example of such language (see MPEP 2106 II). Since the invention of Stroganov et al. and the invention as claimed are the same, the invention of Stroganov et al. would be capable of performing the intended use of providing an yttrium concentration in the region of the human smooth muscle cells to be treated of between 200 uM and 2 mM, in particular between 800 uM and 1 mM, as taught by claim 15.

Response to Arguments

13. Applicant's arguments filed 6/5/08 have been fully considered but they are not persuasive.

Applicants first argue the rejection ignores the clear limitations of claim 4, which has been amended to additionally reinforce the wording of the claim to indicate that the implantation in a vascular vessel, the adaptation of the composition for inhibition of smooth muscle cell proliferation and intravascular liberation of the composition is not optional.

This argument is not persuasive because the above cited claim language is drawn to the intentional uses of the composition. The language of the claim directed to implantation in a vascular vessel, inhibition of smooth muscle cell proliferation and intravascular liberation does not impart any structural limitation to the composition, and therefore does not add anything that is not already present in the composition. All of the elements recited in the claim are found in the disclosure of Stroganov et al, and therefore the reference anticipates the claims.

Applicants also argue that Stroganov indicates that their composition stimulates the proliferation of bone tissue, and does not provide any teaching or suggestion that an alloy of this composition is suitable for implantation in a vascular vessel under any conditions.

This argument is not persuasive because Stroganov does not teach away from the inhibition of proliferation of smooth muscle cells, or exclude its composition from being used for such purposes. On the contrary, the composition has pharmaceutical purposes and does not contain elements which are harmful for the living organism (see col. 2, lines 13-15). As such, since the invention of Stroganov et al. and the invention as claimed are the same, the invention of Stroganov et al. would be capable of performing the intended uses recited in the "adapted for" clauses of the claimed invention, absent evidence to the contrary.

Applicants further argue that Stroganov provides no teaching or suggestion of the delivery of yttrium to smooth muscle cells at the levels recited by claim 15, and that claim 15 does not treat as optional the delivery of yttrium to smooth muscle cells to be treated.

This argument is not persuasive. Claim 15 is not a method claim with positive method steps, but a composition claim. The "adapted for" language of claim 15 does not impart any structural limitation to the claim, nor does it limit the scope of the claim.

Since the invention of Stroganov et al. and the invention as claimed are the same, the invention of Stroganov et al. would be capable of performing the intended use of providing an yttrium concentration in the region of the human smooth muscle cells to

be treated of between 200 uM and 2 mM, in particular between 800 uM and 1 mM, as taught by claim 15.

Claim Rejections - 35 USC § 103

14. Claims 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stroganov et al (US Patent 3,687,135).

The claimed invention and the invention of Stroganov et al. are recited above (see paragraph 13).

With respect to claims 12-14, Stroganov et al do not exemplify a formulation comprising a magnesium alloy and containing Y, rare earths without Y, and remaining elements, or containing, Y, Nd, and Zr, in the weight percentages specified by claims 12-14.

However, Stroganov et al do teach that the rare earth metals (i.e., Y plus rare earths without Y, or Y and Nd) in the range of 0.4 – 4.0 wt.%. Additionally, Stroganov et al teach that zirconium may be present in amount ranging from 0 – 0.8 wt.%, and the total remaining elements may be present in amounts ranging from 0.15 – 5.1 wt.% (col. 2, lines 20-28). These ranges overlap those of the claimed invention (note that the amount of yttrium of "about 4.1%" in claim 14 reads on "4.0%" in Stroganov et al), and one skilled in the art would be motivated to select optimal amounts of the elements from within said ranges by routine experimentation in order to control the rate of absorption of the magnesium alloy carrier (for example, see col. 1, lines 58-60). Stroganov et al also

teach that neodymium and yttrium are predominantly employed as the rare earth metal (col. 2, lines 29-31).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to form a pharmaceutical formulation having the elements and amounts as specified by the claimed invention with a reasonable expectation of success.

It is prima facie obvious to combine two compositions, each of which is taught by the prior art, to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. See MPEP 2144.06. One skilled in the art would have been motivated to combine the compositions comprising yttrium and neodymium as the rare earth metal, since alloys, by their nature, are known to have improved properties with a combination of elements, with a reasonable expectation of success. Additionally, one skilled in the art would have been motivated to select zirconium to be present in the formulation, since zirconium is already exemplified in the formulations of Stroganov et al.

Response to Arguments

15. Applicant's arguments filed 6/5/08 have been fully considered but they are not persuasive.

Applicants argue that Stroganov teaches away from the present invention by providing a composition that stimulates cell growth instead of inhibiting it, and because the purpose of Stroganov is not the very same purpose as that of the present invention,

but rather the complete opposite, i.e., Stroganov's composition stimulates cell growth, while the claimed invention inhibits it.

This argument is not persuasive because, as stated previously, Stroganov teaches that its compositions can be used to stimulate bone growth, but it does not exclude its compositions from being used for the inhibition of proliferation of smooth muscle cells. Since the invention of Stroganov et al. and the invention as claimed are the same, the invention of Stroganov et al. would be capable of performing the intended uses recited in the "adapted for" clauses of the claimed invention, absent evidence to the contrary.

Applicants also argue that if one were to combine the compositions of Stroganov, Stroganov provides an upper limit of total rare earth metals of 4.0% by weight, while the claimed invention provides a total rare earth weight percentage of 5.2%, (claim 12), 5.5% (claim 13), or 6.3% (claim 14).

This argument is not persuasive because it would still be prima facie obvious to person having ordinary skill in the art combine the compositions comprising yttrium and neodymium disclosed by Stroganov for the, since both compositions would be useful for the same purpose disclosed by Stroganov (noting that the composition thus formed still anticipates the claimed invention, for reasons stated above), and such a combination would reasonably be expected to improve the control of adsorption of the magnesium alloy carrier (see col. 1, lines 58-60). The combination of compositions comprising yttrium and neodymium is not limited to the weight range specified in Stroganov, since the weight ranges specified in Stroganov are limited to the individual compositions.

Claim Rejections - 35 USC § 112

16. **Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.** The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 14 now recites the formulation for WE43, as suggested by the Examiner in the Examiner's Remarks of the previous Office action. However, claim 14 includes the term "about" before the weight percentage or each element (see lines 3-6). Said language does not appear in the specification (see paragraph [0048] of the specification), and thus claim 14 includes subject matter not described in the specification.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 9am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611